the <u>same</u> components, as recited in the above expression vector, and the expression cassette and vector containing it, as claimed in the patent. (Underscoring provided).

As submitted during the interview, the expression cassette claimed herein does not comprise the same components as the claims of '479. A review of the claims of patent '479 shows that the underscored words in claim 2 (amended) and in the independent claims are not present in the claims of the '479 patent. See the sentence the "chloroplast DNA sequences which originate from a plant species the same as or different from the target plant, said sequences being conserved in all higher plants and complementary to the corresponding chloroplast sequences of the target plant, which sequences are also competent of undergoing homologous recombination with said complementary sequences of the target plant".

These features are neither called for in the claims nor described in the specification of '479. There is no teaching or suggestion that chloroplast DNA sequences and the complementary corresponding chloroplast sequences of the target plant are competent of undergoing homologous recombination with said complementary sequence of the target plant.

Accordingly, this rejection on this patent is respectfully traversed.

# The Double Patenting Rejection on Patent Application 09/972,901

The identified claims listed in the Office Action are rejected on the claims of patent application '901. Reasons are stated on pages 7-8 of the Office Action.

Like in the previous remarks with respect to the issued patent '479, the same features which were noted above in the generic claims of this patent application do not contain the <u>same</u> components as the claimed vector in this '901 patent application. There is no teaching or suggestion in '901 for the words which are underscored in claim 2 (and the other claims identified above) and these sequences are not identified in the '901 patent application. Accordingly, it is submitted that the rejection on application '901 should be withdrawn.

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### The Double Patenting Rejection on Patent Application 09/356,192

The claims 31-85, 118-119 and 122 of this application are rejected over claims 1, 2, 5 and 6 of copending application no. 09/356,192. The reasons are stated on pages 7-8 of the Office Action.

The elements underscored in the claims like claim 2 (and in the other independent claims) are not suggested or obvious in the claims of the '192 patent application. Accordingly, it is submitted that the double patenting rejection on application '192 is to be withdrawn.

There is no feature of the universal vector claimed in the instant application which is taught or suggested in the cited '479, the applications '901 or '192. See the discussion of the prior art in this application on pages 4-6. The art taught away of the universal vector. See also the Amendment filed on October 26, 2000. The universal vector is contrary to the dogma for lack of conservation of the spacer region 2. See specification on page 8, paragraphs 1 and 2, pages 9-11.

## II. The Rejection on the Prior Art

The rejection of the identified claims on Staub et al. (1993) in light of Staub (1992) in the Office Action, page 13 under 35 USC §102(b) is also traversed. Remarks were submitted in the earlier amendment filed October 26, 2000. At the interview, it was proposed that the undersigned was to provide additional comments on these references, which the undersigned is pleased to submit. Both under 35 USC §102(b) and 35 USC §103(a) are discussed herein.

Staub et al. (1992 and 1993) also do not anticipate the universal vector. The pJS75 vector is not identical to the Universal Vector ("UV") and does not possess an expression cassette that is the same as the expression cassette in uV. Thus, there is no basis for a 35 USC §102 rejection. However, pJS75 does contain the spacer2 region along with additional chloroplast sequences, but the spacer2 region does not appear to

be instrumental in the recombination reactions that are directed by pJS75. There are also many differences between pJS75 and uV.

In the 1993 paper, Staub et al. discusses the regulation of D1 accumulation. A chimeric uidA gene encoding GUS was integrated into the tobacco plasmid genome. The chimeric uidA gene was cloned between the trnV gene and ribosomal RNA operon in vector p1575, to create plasmid p1580. Page 601, under Results, lines 5-7. The chimeric uidA gene was cloned into Dral site of p1575 between the trnV and 165r DNA genes. See Fig 1A, page 602; see bottom line trnV\_\_\_\_\_ 5psb A/uidA/psBA3'\_\_\_\_\_\_ 16Sr DNA\_\_\_\_\_. Compare this region (between trnV gene and the 16Sr DNA gene) with the region of the intergenic spacer 2 region between tRNA lia and the tRNA lia genes of the chloroplast gene, claim 4. And compare this region with the region which is flanking DNA sequences which are homologous to a spacer sequence of the target chloroplast gene.... Claim 2.

Staub et al insert sequences between trnV and 16S RNA, not in the spacer2 region between trnA and trnI. Because of this, Staub is relying on trnV and 16S RNA to direct homologous recombination rather than on trnA and trnI, as in this application. There is no indication of the utility of the spacer2 region to direct homologous recombination in this Staub paper. In addition, pJS75 possesses chloroplast sequences derived from tobacco and the plasmid is used only to transform tobacco. There is no teaching to use pJS75 to transform plant species other than tobacco. Therefore, two essential properties of uV, the use of spacer2 to direct recombination and the ability of spacer2 to recombine with many plant species, are not anticipated or obvious from the Staub et al. references. In summary, there is no teaching of universal transformation of plants using spacer2 as a targeting (flanking) sequence. Staub 1993 simply teach transformation of tobacco with a vector containing trnV and 16S RNA flanking sequences derived from tobacco.

The 1992 paper also describes the pJS75 vector and thus is limited to the transformation of tobacco cells by homologous recombination by sequencew derived

from tobacco. There is no universal transformation capability shown. In addition, this paper also does not even provide an example of a vector containing an expression cassette with a heterologous sequence. The goal of this paper is to demonstrate that stable transformation of tobacco chloroplasts occurs using a vector possessing chloroplast sequences derived from tobacco. The Examiner states that the pJS75 vector of Staub inherently possesses spacer2, and that is true. But there is no teaching, suggestion or demonstration that spacer2 alone can function as a targeting sequence to induce homologous recombination. Indeed, Staub et al. state in the title of the paper and in the Abstract that "the integration of long uninterrupted regions of homologous DNA, rather than small fragments..., is the more likely event in plastid transformation of land plants." Thus, Staub et al (1992) teach that long sequences are necessary for directing homologous recombination, not short sequences like spacer2. This does not anticipate or make obvious the uV of the present invention. Indeed, Staub directs the skilled artisan to use long targeting sequences for transformation and leads the skilled artisan away from using a small targeting sequence like spacer2.

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Furthermore, examination of the recombinant tobacco calli obtained using pJS75 indicates that the spacer2 region was not instrumental for directing homologous recombination and indeed, the spacer2 region is not even present in some of the recombinant plants generated in their experiments. For example, product PT9 which is generated by transformation of tobacco with pJS75 is shown not to possess an XbaI site (Discussion pg, 42, column 2, line 4, also see Figure 1). The Xbal site is located in spacer2 (see Figure 1 of Staub, 1992). This clearly shows that spacer2 was either not involved in the homologousd recombination or alternatively, was unstable in the transformed plants. In either case, the skilled artisan is lead even further away from using spacer2 as a targeting sequence since it may be non-functional or unstable in the transformed products. In contrast, the uV of the present invention clearly shows that spacer2 directs stable homologous recombination not only with tobacco but with many other plant species. Based on the findings of Staub et al. 1992 and 1993, this s an

unanticipated and unexpected result. There is no basis for the rejections, it is submitted by the Examiner.

#### III. The Claims to the Transported Plant

Claims 118 and 122 drawn to the transformed plants are rejected under 35 USC §102(b) as anticipated or in the alternative of 35 USC §103(a) as obvious over Zoubenko and Biotechnica. The rejection is addressed in the previous Amendment on pages 21 and 23.

Claims 118 and 122 are dependent on claim 4. As submitted in the interview with the Examiner, the plants differ over the prior art not only by the method of making them, but also that the chloroplast genome comprises a portion of the intergenic spacer 2 region between the tRNA<sup>lic</sup> and the tRNA<sup>Ala</sup> genes of the chloroplast genome. It is to be noted that claims 119 and 122 are also indirectly included by the features of claim 2. See the underscored portion of claim 2. These features are not identified in the two primary references, namely, the use of an expression vector which comprises two tRNA genes and intergenic spacer 2 region. Further, unlike what the Examiner states, the use of said expression vector does confer the property to the transform chloroplasts or plants. The recombination does result in the introduction of the new sequences in the target plant. See page 23 of the Amendment (other than the heterologous DNA of interest). Further, the transformed plant can generate a progeny which contains the same sequences as the transformed parent plant. See claims 20 and 21.

Accordingly, the rejection of these transformed plants is respectfully requested to be withdrawn.

### Conclusion

The invention has made a worthwhile contribution to the art of agriculture. It is submitted that this patent application is in condition for allowance. In the event that there should be any additional questions, the Examiner is invited to call the undersigned at the telephone number indicated.

Respectfully submitted,

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For SCHNADER HARRISON SEGAL & LEWIS LLP 215-751-2427